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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

MARVICH, MARIA

ART UNIT

PAPER NUMBER

1636

DATE MAILED: 11/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/762,648	Applicant(s) JARRELL ET AL.	
	Examiner Maria B Marvich, PhD	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 July 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-36 is/are pending in the application.
- 4a) Of the above claim(s) 11,24-29 and 31-36 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 19 is/are allowed.
- 6) ☒ Claim(s) 1-10,12-18,20-23 and 30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 15 April 2001 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|--|
| <p>1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)</p> <p>2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)</p> <p>3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____</p> | <p>4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____</p> <p>5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)</p> <p>6) <input type="checkbox"/> Other: _____</p> |
|---|--|

DETAILED ACTION

This office action is in response to a Response to a Restriction Requirement filed 7/6/04.

Claims 1-36 are pending in the application.

Election/Restrictions

Applicant's election without traverse of Group I (claims 1-10, 12-23 and 30) in the amendment filed 7/6/04 is acknowledged. Therefore, Claims 11, 24-29 and 31-36 are withdrawn as drawn to non-elected subject matter. Claims 1-10, 12-23 and 30 are examined in this office action in as much as they read on a transcriptional regulator comprised of RNA that increases transcription.

Drawings

Figure 4 is objected to under 37 CFR 1.83(a) because it fails to show any details as described in the specification. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). The figure is a photograph of a Northwestern blot. However, the image is black with no discernible bands. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Claim Objections

Claims 1-9, 11-23 and 30 are objected to because of the following informalities: the claims are drawn to non-elected subject matter. Appropriate correction is required.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 5-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 is vague and indefinite in that the metes and bounds of “similarly-positioned site” are unclear. By reciting that Gal4 activates transcription from a “similarly-positioned site”, the relationship between the DNA site and the ability of Gal4 to activate transcription from the promoter is unclear. As Gal4 does not activate transcription from any site, it is unclear how a “similarly-positioned site” would lead to the ability of Gal4 to activate transcription from any promoter such that the levels of Gal4 activated transcription is comparable to activation by the transcriptional regulator comprised of RNA.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 1-10, 12-23 and 30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to a transcriptional regulator comprised of a DNA binding moiety and an RNA linked to the DNA binding moiety, the RNA having transcriptional regulatory activity.

The written description requirement for genus claims may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with known or disclosed correlations between function and structure, or by a combination of such characteristics sufficient to show that the applicant was in possession of the claimed genus.

The instant invention is drawn to transcriptional regulator, which demonstrates specific DNA activity by virtue of nucleic acids, polypeptides, intercalation compounds and chemicals. The disclosure provides a screening method for identification of RNA molecules that are regulators of transcription by using a variation of a Wickham Field screen. In the instant screen, a *lexA* DNA binding moiety is linked to an MS2 coat protein, which interacts with MS2 RNA, linked to bait RNA. Bait RNA molecules that can activate or inhibit transcription are thus identified (see e.g. page 14, last paragraph). Several isolates are identified and these isolates have a consensus sequence (SEQ ID NO:4). In the absence of the *lexA*-MS2 hybrid, the

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riboactivators did not activate transcription (see e.g. page 25, last paragraph). Applicants only exemplify transcriptional regulators that by virtue of the screen are in association with *lexA* DNA binding moieties. Therefore, applicants have not reduced to practice the claimed invention as regards transcriptional regulators that are comprised of DNA binding moieties that are polypeptides, intercalation compounds and chemicals that demonstrate specific binding. While numerous polypeptides, intercalation compounds and chemicals may mediate DNA binding, it is unclear whether any of these mediate specific binding. Applicants provide no examples of DNA binding moieties that would meet the requirements of the instant invention. Furthermore, applicants do not reduce to practice a regulator whose activity is squelched by over expression of Gal4. As applicants do not provide an example of the riboregulator, the relationship between structure of a riboregulator and its ability to be squelched by over-expression of Gal4 is unknown. Given the widely divergent nature DNA binding moieties and the uncertainty of the specific DNA binding, it must be considered that riboregulator according to the instant invention with DNA binding activity must be empirically determined. In an unpredictable art, the disclosure of one example would represent to the skilled artisan that applicants were not in possession of claimed genus. Furthermore, given the widely divergent nature of RNA molecules that might function as RNA regulators and the inability to determine which would be squelched by over expression of Gal4, it must be considered that riboregulator according to the instant invention must be empirically determined. In an unpredictable art, the disclosure of no examples would represent to the skilled artisan that applicants were not in possession of claimed genus.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 6-8, 10, 12-15, 20, 21 and 23 are rejected under 35 U.S.C. 102(a) as being anticipated by Svinarchuk et al (NAR, 1997, Vol 25917) pages 3459-3464.

Svinarchuk et al teach a transcriptional regulator comprised of RNA. The regulator is a hairpin oligoribonucleotide, SRE-TFO, that is able to recruit transcription factors to the target DNA sequence. SRE-TFO is a bi-functional molecule that contains a stem and loop structure that is greater than 10 base pairs that recruits transcription factors such as SRF and ELK and a TFO DNA binding moiety (see e.g. figure 1A and page 3459, col 2, paragraph 2). The regulator SRE-TFO modulates transcription of the SIV *vpx* gene by activating initiation (see e.g. page 3463, col 2, paragraph 2). As transcription results, the TFO functions by effecting all stages of transcription such as initiation, elongation, and termination. The SIV *vpx* regulation would occur in host cells for SIV such as non-human simians. The DNA binding moiety is comprised of nucleic acid. While claim 23 recites a transcriptional regulator identified by expression of a linked library and detection of a change in transcription, it is not clear that the transcriptional regulator identified by the method of claim 23 differs from the transcriptional regulator taught by Svinarchuk et al. Because the Office does not have the facilities for examining and comparing the applicant's product with the products of the prior art, the burden is on the applicant to show a

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novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See in re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Claims 1-3, 12-17, 21, 23 and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Postel et al (PNAS, 1991, Vol 88 pages 8227-8231).

Postel et al teach use of a transcriptional regulator comprised of RNA. The regulator is a 27 base pair oligoribonucleotide called PUI that binds tightly to *c-myc* promoter (see e.g. page 8227, col 1, paragraph 2). The DNA binding moiety is comprised of nucleic acid. PUI is introduced into Hela cells and blocks transcription (see e.g. figure 5). As transcription does not occur, the TFO functions by effecting all stages of transcription such as initiation, elongation, pausing and termination. The transcriptional regulator is dissolved in water and can therefore be considered a therapeutic composition in a pharmaceutically acceptable carrier. While claim 23 recites a transcriptional regulator identified by expression of a linked library and detection of a change in transcription, it is not clear that the transcriptional regulator identified by the method of claim 23 differs from the transcriptional regulator taught by Postel et al. Because the Office does not have the facilities for examining and comparing the applicant's product with the products of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See in re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

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Claims 1-4, 10, 12, 15-18, 21, 22 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhang et al (JVI, 1994, Vol 68(8), pages 4738-4746; see entire document).

Zhang et al teach a transcriptional regulator comprised of RNA. The regulator is the MHV leader sequence containing two UCUSA repeats which initiates transcription of multiple MHV genes (see e.g. page 4740, col 2, paragraph 4 and page 4738, col 1, paragraph 1). DBT cells, mouse astrocytoma derived cells were infected with constructs comprising the leader sequence and transfected with constructs comprising initiation sequences (IS) fused to a CAT reporter gene. The leader sequence is conditionally active depending upon infection of the MHV and expression of the leader upon which expression of CAT increased 4-37 fold with IS-2-1 and 291-306 with IS-7 (from strain MHV) (see e.g. table 1 and page 4739, col 2, paragraph 3-4). The interaction of the leader sequence with the DNA leads to increased initiation (see e.g. figure 5). As transcription results, the TFO functions by affecting all stages of transcription such as initiation, elongation and termination. While claim 23 recites a transcriptional regulator identified by expression of a linked library and detection of a change in transcription, it is not clear that the transcriptional regulator identified by the method of claim 23 differs from the transcriptional regulator taught by Zhang et al. Because the Office does not have the facilities for examining and comparing the applicant's product with the products of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See *in re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Conclusion


Claim 19 is allowed.

Claims 1-10, 12-18, 20-23 and 30 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD can be reached on (571)-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


GERRY LEFFERS
PRIMARY EXAMINER

Maria B Marvich, PhD
Examiner
Art Unit 1636

October 27, 2004